

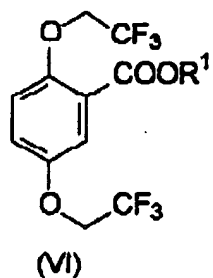
- 5 -

**AMENDMENTS TO THE CLAIMS**

Please amend the claims as follows:

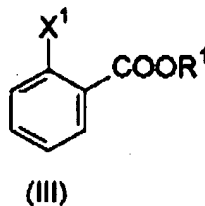
1. (currently amended) Process for the preparation of Flecainide, as Flecainide base or any pharmaceutically acceptable salts thereof, comprising:

preparation of a compound of formula VI



wherein R<sup>1</sup> is H, alkali metal or a C<sub>1</sub> to C<sub>9</sub> alkyl group;

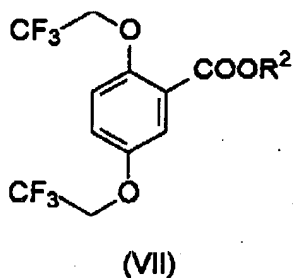
from compounds of formula III



wherein X<sup>1</sup> is F, Cl, Br or I and R<sup>1</sup> is H, alkali metal or a C<sub>1</sub> to C<sub>9</sub> alkyl group;

optional conversion of the compound of formula VI to the ester of formula VII by reacting with a hydroxyl compound R<sup>2</sup>OH;

- 6 -



wherein R<sup>2</sup> is C<sub>1</sub> to C<sub>9</sub> alkyl group, aryl group or succinimidyl;

amide formation of the compound of formula VI or VII forming flecainide base by reacting with 2-(aminomethyl)piperidine and;

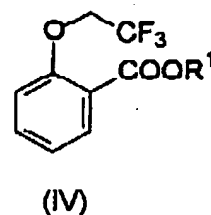
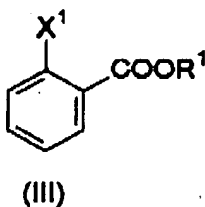
optionally forming a pharmaceutically acceptable salt thereof.

2. (cancelled)

3. (cancelled)

4. (currently amended) Process for the preparation of Flecainide, as Flecainide base or any pharmaceutically acceptable salts thereof, comprising

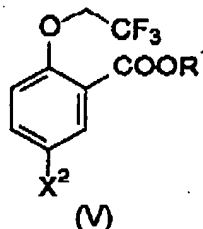
reaction of the ~~2-halo~~benzoic acid derivatives compounds of formula III with an alkali or alkaline earth metal alkoxide of 2,2,2-trifluoroethanol in the presence of a copper-containing catalyst comprising cupric chloride, cupric bromide, cupric iodide, cuprous chloride, cuprous bromide, cuprous iodide, copper (I) oxide, copper (II) oxide or copper-zinc alloy, in a solvent to form ~~2-(2,2,2-trifluoroethoxy)benzoic acid derivatives~~ compounds of formula IV;



- 7 -

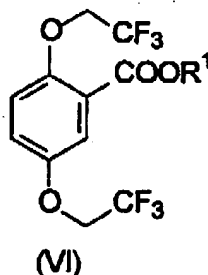
wherein  $X^1$  is F, Cl, Br or I and  $R^1$  is H, alkali metal or a  $C_1$  to  $C_9$  alkyl group;

halogenation of the compounds of formula IV to form 5-halo-2-(2,2,2-trifluoroethoxy)benzoic acid derivatives of formula V;



wherein  $X^2$  is Cl, Br, or I [[.]] and  $R^1$  is H, alkali metal or a  $C_1$  to  $C_9$  alkyl group;

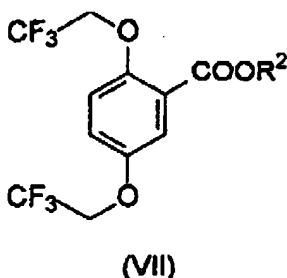
reaction of the compounds of formula V with an alkali or alkaline earth metal alkoxide of 2,2,2-trifluoroethanol in the presence of a copper-containing catalyst comprising cupric chloride, cupric bromide, cupric iodide, cuprous chloride, cuprous bromide, cuprous iodide, copper (I) oxide, copper (II) oxide or copper-zinc alloy, in a solvent to form compounds of formula VI;



wherein  $R^1$  is H, alkali metal or a  $C_1$  to  $C_9$  alkyl group;

optional conversion of the compounds of formula VI to a new ester of formula VII by reacting with hydroxyl compound  $R^2OH$ ;

- 8 -



wherein R<sup>2</sup> is C<sub>1</sub> to C<sub>6</sub> alkyl group, aryl group or succinimidyl;

selective amide formation by reacting compounds of formula VI or VII with 2-(aminomethyl)piperidine forming flecainide base;

optionally forming a pharmaceutically acceptable salt thereof.

5. (original) The process of Claim 4 wherein either solvent comprises a polar solvent.
6. (original) The process of Claim 4 wherein the pharmaceutically acceptable salt is the monoacetate salt.
7. (original) The process according to Claim 4, wherein the alkali or alkaline earth metal alkoxide of 2,2,2-trifluoroethoxide is sodium, potassium, calcium or lithium 2,2,2-trifluoroethoxide.
8. (previously presented) The process according to Claim 4, wherein the alkali or alkaline earth metal alkoxide of 2,2,2-trifluoroethanol is synthesized by reacting 2,2,2-trifluoroethanol with a base selected from potassium *tert*-butoxide, sodium *tert*-butoxide, sodium isopropoxide and sodium methoxide.
9. (cancelled)
10. (cancelled)
11. (original) The process according to Claim 4, wherein X<sup>2</sup> is Br.

- 9 -

12. (original) The process according to Claim 4, wherein  $R^2$  is selected from methyl, ethyl, benzyl and phenyl.

13. (original) The process according to Claim 4, wherein the compound of formula VI or VII is 2,5-bis-(2,2,2-trifluoroethoxy)benzoate.

14.(original) The process according to Claim 13 wherein any of the reactions is carried out in aliphatic, cycloaliphatic or aromatic solvents from 5 to 10 carbon atoms or ethers from 4 to 10 carbon atoms.

15. (previously presented) The process according to Claim 14, wherein the solvents comprise hexane, heptane, cyclohexane, tetrahydrofuran, 1,2-dimethoxyethane, diethyleneglycol dimethyl ether, toluene, xylene, or acetonitrile.

16. (original) The process according to Claim 13, wherein the reaction temperature is between 0°C to 150°C.

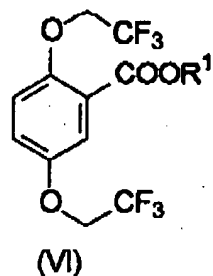
17. (original) The process according to Claim 13, wherein the temperature is between 50°C to 120°C.

18. (original) The process according to Claim 13, wherein the molar ratio between 2,5-bis-(2,2,2-trifluoroethoxy)benzoate and 2-aminomethylpiperidine is from 1:1 to 1:2.

19. (original) The process according to Claim 18, wherein the molar ratio is from 1:1 to 1:1.5.

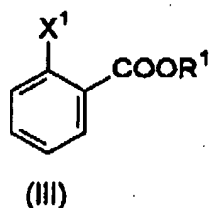
20. (currently amended) The process for the preparation ~~benzoic acid derivatives of~~ compounds of formula VI ;

- 10 -



wherein R<sup>1</sup> is H, alkali metal or a C<sub>1</sub> to C<sub>9</sub> alkyl group;

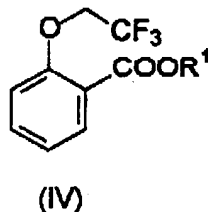
from compounds of formula III



wherein X<sup>1</sup> is F, Cl, Br or I and R<sup>1</sup> is H, alkali metal or a C<sub>1</sub> to C<sub>9</sub> alkyl group;

comprising:

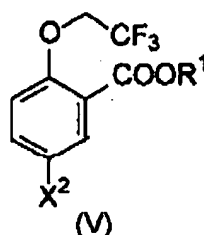
reaction of compounds of formula III with an alkali or alkaline earth metal alkoxide of 2,2,2-trifluoroethanol in the presence of a copper-containing catalyst comprising cupric bromide, cupric iodide, cuprous chloride, cuprous bromide, cuprous iodide, copper (I) oxide, copper (II) oxide or copper-zinc alloy, in a solvent to form compounds of formula IV;



wherein R<sup>1</sup> is H, alkali metal or a C<sub>1</sub> to C<sub>9</sub> alkyl group;

- 11 -

halogenation of the compounds of formula IV to form compounds of formula V;



wherein  $X^2$  is Cl, Br, or I and  $R^1$  is H, alkali metal or a  $C_1$  to  $C_6$  alkyl group;

reaction of compounds of formula V with an alkali or alkaline earth metal alkoxide of 2,2,2-trifluoroethanol in the presence of a copper-containing catalyst comprising cupric bromide, cupric iodide, cuprous chloride, cuprous bromide, cuprous iodide, copper (I) oxide, copper (II) oxide or copper-zinc alloy, in a solvent.

21. (original) The process according to Claim 20 wherein either solvent comprises a polar solvent.

22. (original) The process according to Claim 20, wherein the alkali or alkaline earth metal alkoxide of 2,2,2-trifluoroethoxide is sodium, potassium, calcium or lithium 2,2,2-trifluoroethoxide.

23. (previously presented) The process according to Claim 20, wherein the alkali or alkaline earth metal alkoxide of 2,2,2-trifluoroethoxide is synthesized by reacting 2,2,2-trifluoroethanol with a base selected from potassium *tert*-butoxide, sodium *tert*-butoxide, sodium isopropoxide and sodium methoxide.

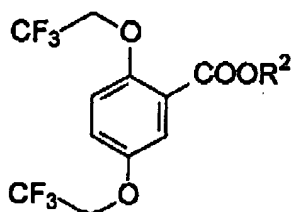
24. (cancelled)

25. (cancelled)

26. (original) The process according to Claim 20, wherein  $X^2$  is Br.

- 12 -

27. (currently amended) The process for the preparation of Flecainide from ~~2,5-bis(2,2,2-trifluoroethoxy)benzoic acid derivatives~~ compounds of formula VII,



(VII)

wherein R<sup>2</sup> is methyl, ethyl, propyl, butyl, benzyl, phenyl or succinimidyl;

comprising the selective amide formation by reacting the ~~benzoic acid derivative compound~~ of formula VII with 2-(aminomethyl) piperidine.

28. (original) The process according to Claim 27, wherein the reaction is carried out in aliphatic, cycloaliphatic or aromatic solvents from 5 to 10 carbon atoms or ethers from 4 to 10 carbon atoms.

29. (previously presented) The process according to Claim 27, wherein the reaction is carried out in solvents and the solvents are selected from hexane, heptane, cyclohexane, tetrahydrofuran, 1,2-dimethoxyethane, diethyleneglycol dimethyl ether, toluene, xylene, acetonitrile.

30. (previously presented) The process according to Claim 28, wherein the solvent is toluene or xylene.

31. (original) The process according to Claim 27, wherein the reaction temperature is between 0°C and 150°C.

32. (original) The process according to Claim 27, wherein temperature range is between 50°C and 120°C.



- 13 -

33. (original) The process according to Claim 27, wherein the molar ratio between the benzoic acid derivative and 2-aminomethylpiperidine is from 1:1 to 1:2.

34. (original) The process according to Claim 33, wherein the molar ratio is from 1:1 to 1:1.5.

35. (original) 5-Bromo-2-(2,2,2-trifluoroethoxy)benzoic acid.